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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,615	07/10/2001	Avi Ashkenazi	10466/65	9850

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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

KC

Office Action Summary	Application No.	Applicant(s)	
	09/902,615	ASHKENAZI ET AL.	
	Examin r	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1 136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachm nt(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *07222003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Part III: Detailed Office Action

Claims 39-43 are pending and under consideration. Applicants statement that claims 52-53 have been cancelled is not pertinent, as there appear not to have been such claims present in the case at any time.

Priority Determination:

In the previous Office Action, it was stated that priority is granted only to the instant filing date, 7/17/01, based upon the lack of utility and enablement of the claimed subject matter. In response to this finding, applicants have argued that they are relying on the results of the Skin Vascular Permeability Assay (Example 77) to establish priority, and that such may be found in PCT/US98/19437, filed 17 Sept. 1998. This argument has been fully considered, but is not deemed persuasive for reasons below in the consideration of applicants traversal of the rejection for lack of utility under 35 U.S.C. § 101. Priority stands at the instant filing date, 7/17/01.

Double Patenting Rejections:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 39-43 remain are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 09/904786. The Examiner appreciates Applicants' having pointed out the

correct Serial Number. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to antibodies that bind PRO335, which is 100% identical to SEQ ID NO: 294 from residue 20 to the terminus. Accordingly, PRO326 and PRO335 appear to differ only in their signal sequences, and the claims are coextensive as antibodies that bind one would largely also bind the other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants traverse that the rejection is moot, as they have already filed a terminal disclaimer in the copending application. This argument has been fully considered but is not deemed persuasive because there is no assurance that this will be the first of the two to issue as a patent. Accordingly, a terminal disclaimer is also required in *this* application.

Formal Matters:

The new title of the invention is acknowledged.

Objections and Rejections under 35 U.S.C. §101 and 112:

35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 39-43 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for reasons of record in the previous Office Action. Applicants traversal of this rejection has been fully considered but is not deemed persuasive for reasons as follow:

Applicants rely on the positive reaction obtained in a skin vascular permeability assay as establishing utility for the claimed antibodies. Applicants argue that the protein encoded by PRO326 caused an inflammatory reaction, and that such inflammatory reactions have been used to characterize cytokines such as IL8, and that thus "a variety of real-life utilities are envisioned for PRO326 based upon the proinflammatory cell infiltration assay results". The Examiner is somewhat confused by applicants argument, as it is not clear what "variety of real-life uses" is envisioned, and applicants have

not specifically enumerated such. Applicants therefore conclude that because PRO326 caused a toxic reaction, that antibodies against PRO326 are useful for treating inflammation, thus meet the utility and enablement provisions of 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph. This argument has been fully considered but is not deemed persuasive because use to induce inflammation is not considered to be a substantial, real-world use. All that the vascular permeability assay establishes is that the substance applied is an irritant. While particular irritants may have uses that stem from that irritant capability, in the absence of further characterization of what type of reaction the substance causes and what the systemic effects of such are, the result remains a preliminary one, necessitating substantial further research to determine an actual, real-world use for the compound. For example, the Rampart reference (Am. J. Pathol. 135:21, 1989) cited by applicants in their response is one in which IL-8 was found to induce plasma leakage and neutrophil accumulation in rabbit skin (title). Rampart et al. did not merely assay the types of cells attracted, but also looked at the kinetics of the reaction, and concluded that based upon the *kinetics* of the responses, which were similar to those induced by C5a and FMLP, that "IL-8, if produced endogenously, may be involved in the acute phase of an inflammatory response to a microbial stimulus". Such is a speculative conclusion, and clearly would indicate to the person of ordinary skill in the art that the authors envisioned that substantial further work would have been required to confirm that speculation. In this specific case, human PRO326 was found to be an irritant to guinea pigs. Such *might* indicate that PRO326 is an inflammatory cytokine (although based on such a result, the person of ordinary skill in the art would not consider that to be a supportable conclusion), or alternatively it might indicate that the guinea pigs are allergic to PRO326, e.g. that the human PRO326 protein has an epitope that the guinea pigs were pre-sensitized to. In either case, as was the case in the Rampart et al. publication, the observation is merely a jumping-off point, that is, an invitation to experiment further to determine the properties of PRO326. Accordingly, the only inflammation that could be treated using anti-PRO326 antibodies at the time the invention was made is that actually caused by PRO326, which is a circular exercise with no meaning (as there is no reason to believe that any patient has any condition resulting from excess PRO326 based upon the results in the specification as originally filed), and does not constitute a substantial utility. It remains that the skin vascular permeability assay does not give sufficient information so as to inform one of skill in the art as to what utility the protein encoded by the claimed nucleic acids might have, nor how to use such.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-43 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 is indefinite because an antibody cannot be a fragment of itself. Applicants have traversed that they are permitted to be their own lexicographer. This argument has been fully considered but is not deemed persuasive because while applicants may coin their own terms and define them, hence engaging in lexicography, applicants are not permitted to use ordinary terms in novel ways, giving them other than their accepted definitions. It remains that an "antibody" cannot *be* a "fragment of an antibody". The whole cannot be a fragment of itself.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the

invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39-43 remain rejected under 35 U.S.C. 102(e) as being anticipated by Wu et al., U.S. Patent Number 6,046,030.

U.S. Patent Number 6,046,030 teaches a protein of SEQ ID NO: 5, having 50% identity to residues 1-1083 of SEQ ID NO: 294, and SEQ ID NO: 2, having 49.8% identity to residues 32-1036 of SEQ ID NO: 294. 21 lines 59 to column 22 line 17. Labeled antibodies are disclosed at column 23, lines 42-53. Because of the relatedness of Wu's sequences to those of SEQ ID NO: 294, Wu's antibodies would reasonably be expected to meet the limitations of the rejected claims. Applicants argument that Wu is not applicable as prior art is deemed not persuasive for reasons above regarding the priority date of this application.

Claims 39-44 are rejected under 35 U.S.C. 102(e) as being anticipated by Wang et al., U.S. Patent Number 6,426,072.

U.S. Patent Number 6,426,072 teaches SEQ ID NO: 4, which has 74.8% identity to residues 608-737 of SEQ ID NO: 294.

Antibodies to the proteins, including single chain and humanized antibodies, are disclosed at column 50. Immunoassays using labeled antibodies are disclosed at col. 25. Because of the relatedness of Wang's sequences to those of SEQ ID NO: 294, Wang's antibodies would reasonably be expected to meet the limitations of the rejected claims. Applicants argument that Wang is not applicable as prior art is deemed not persuasive for reasons above regarding the priority date of this application.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A search of the protein sequence databases revealed the following prior art:

Locus	Date	Author	Identity to SEQ ID NO:294
Q9D332	6/1/01	J. Kawai et al.	86% to residues 378-1119
O94898	5/1/99	T. Nagase et al.	58.4% to residues 47-1036
P70193	2/1/97	Y. Suzuki et al.	50% to residues 1-1083

Claims 39-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawai et al. or Nagase et al. or Suzuki et al., any of the three in view of in view of Sibson et al., WO94/01548, for reasons of record in the previous Office Action. Applicants traversal that the claimed antibodies demonstrate an unexpected property in the form of being useful for inhibiting an inflammatory response has been fully considered but is not deemed persuasive for reasons cited above in response to applicants arguments of the rejection under 35 U.S.C. §101. The evidence of record does not support such a use as being a substantial assertion.

Advisory Information:

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

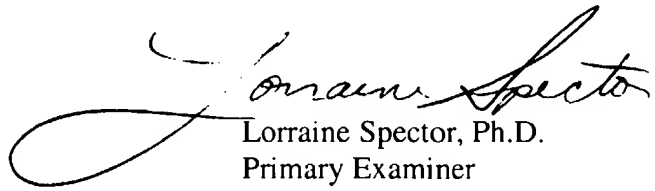
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M. ***Effective 1/21/2004, Dr. Spector's telephone number will be 571-272-0893.***

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623. ***Effective 1/21/2004, Dr. Kunz' telephone number will be 571-272-0887.***

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228. ***Effective 1/21/2004, Dr. Spector's fax number will be 571-273-0893.***



Lorraine Spector, Ph.D.
Primary Examiner